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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/011,977	06/15/1998	HERMANN P.T. AMMON	015200-054	1580

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BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
OWENS JR, HOWARD V	
ART UNIT	PAPER NUMBER
1623	35

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/011,977	AMMON ET AL.	
	Examiner	Art Unit	
	Howard V Owens	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,12-16,18-22,24,25 and 27-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12-16,18-22,24,25 and 27-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

The following is in response to the request for continued examination filed on 6/25/03:

An action on the merits of claims 10, 12-16, 18-22, 24, 25 and 27-40 is contained herein below.

35 U.S.C. 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 12-16, 18-22, 24, 25 and 27-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The instant specification invites the skilled artisan to experiment. The factors which must be considered in determining undue experimentation are set forth in In re Wands 8USPQ 2d 1400. The factors include:

1) quantity of experimentation necessary,
2) the amount of guidance presented,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the predictability of the art,
7) breath of the claims and the
8) level of skill in the art.

Nature of the Invention, State of the Prior Art, Predictability of the Art

The instant claims are drawn to treating the destruction of functional tissue associated with diseases selected from the group consisting of tumors or neoplasms, pulmonary emphysema, acute respiratory distress syndrome, shock lung, cystic fibrosis, chronic bronchitis, etc. in a mammalian organism.

The instant specification does not support the treatment of the destruction of functional tissue associated with diseases selected from the group above in a mammalian organism. The specification supports the inhibition of human leucocytic elastase (HLE) *in vitro*; however, this *in vitro* support is not commensurate to the breadth of mammalian organisms. The specification presents *in vitro* data of HLE inhibition by boswellic acid, however, there is not seen the treatment of the various diseases set forth *in vivo*. Given the variety of factors present in vivo, any claims to treating should provide adequate support for operation of the invention within an *in vivo* environment.

Applicant's statement that "it should be possible to prevent...." does not demonstrate that various mammalian organisms afflicted with the diseases cited supra are administered boswellic acid and there is seen no destruction of functional tissue. Although applicant is not required to reduce to practice the invention as claimed, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, enablement varies inversely with degree of unpredictability of factors involved. The state of the art teaches that "the mere fact that a compound inactivates HLE in vitro is not in itself a guarantee for a physiological role (*Bernstein et al., Progress in Medicinal Chemistry, vol. 31, p. 65, paragraph 2, edited by Ellis et al., 1994)". Thus one of skill in the art could not predict that the variety of diseases could be treated in a mammal based on the *in vitro* inhibition of HLE. Given the state of the art, without adequate support for the treatment of the various diseases cited *in vivo*, the invention as claimed amounts to an invitation to experiment and would result in undue experimentation in the practice of the invention.

35 U.S.C. 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 10, 12-16, 18-22, 24, 25 and 27-40 are rejected under 35 U.S.C. 103 over Ammon et al., EP 0552657 in combination with Mulshine et al., WO 95/24894 and Han, Chin. Med. Sci. J., vol. 9(1), 61-69

The instant claims are drawn to a method of combating diseases selected from the group consisting of chronic bronchitis, glomerulonephritis, rheumatoid arthritis, cystic fibrosis, tumors and neoplasms or tumor metastases which are caused by increased leukocytic elastase or plasmin activity.

The prior art of Ammon et al. has recognized the use of Boswellic acids for the prophylaxis and or control of inflammatory processes that are caused by elevated leucotriene formation and that they inhibit the 5-lipoxygenases. Ammon et al. teach the use of Boswellic acid in the treatment of inflammatory conditions of the joints (rheumatism), bronchitis, chronic hepatitis and chronic asthma (pp. 1-6). Applicant's arguments regarding and whether the mechanism of action by Boswellic acid is dependent upon 5-lipoxygenase inhibition or the concentration of 5-lipoxygenase inhibitors is moot. The prior art has recognized the use of these compounds to treat the same conditions as applicant; therefore, there is no novelty to the invention. However, Ammon does not teach the he use of Boswellic acid as an anti-tumor or anticancer agent. Mulshine et al. teaches the efficacy of 5-lipoxygenase inhibitors in the treatment

of cancer, which adequately bridges the nexus between the differences in the prior art and the invention as claimed with regard to the use of Boswellic acids to treat tumors; moreover, Han further supports the usefulness of Boswellic acid derivatives in the treatment of cancer (see abstract).

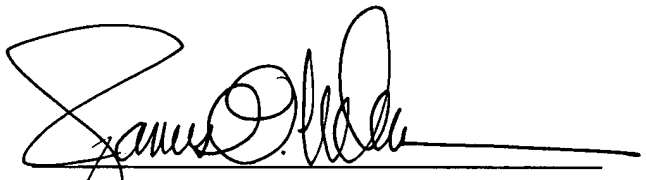
It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use Boswellic acid or a derivative thereof to treat inflammatory processes or neoplasms.

One of skill in the art would have been motivated to use Boswellic acid or plant extracts (such as olibanum) containing Boswellic acid to treat inflammation or neoplasms as the prior art teaches the anti-inflammatory and anticancer activity associated with the use of these compounds. Applicant's connection of Boswellic acid to leukocytic elastase or plasmin activity is considered to be a discovery of one of the pathways affected by Boswellic acid and does not obviate the use of the Boswellic acid in the prior art to treat or combat inflammatory conditions, neoplasms or cancer; moreover, as the prior art has taught the efficacy of 5 lipoxygenase inhibitors in the treatment of cancer or tumors and Boswellic acid has been established in the art as a member of the class of lipoxygenase inhibitors one of skill in the art would have been provided with a reasonable expectation of success in the use of these compounds to treat cancer.

Applicant argues that the prior art had only indicated the use of 5 lipoxygenase inhibitors, such as boswellic acids for the treatment of moderate diseases, such as asthma, and not those of the present invention. However, as cited previously, Ammon et al. teach the use of Boswellic acid in the treatment of inflammatory conditions of the joints (rheumatism), bronchitis and chronic hepatitis which are the same diseases that applicant claims in claim 10 (emphasis added). In the specification, applicants have admitted that the prior art has recognized the ability of the pentacyclic triterpene class of compounds, of which Boswellic acid is a member, (p. 3, lines 14-21) to inhibit human leucocytic elastase (HLE). Although, boswellic acid was not mentioned, one of skill in the art would have a reasonable expectation of success in the use of boswellic acid as an inhibitor of HLE from the multitude of pentacyclic triterpenes since it has been indicated in the prior art as being useful for the same disease conditions associated with HLE, such as rheumatism, bronchitis and chronic hepatitis.

Applicant further argues that inflammation is only one component; however, the examiner maintains the position that is the chief component that is generic to all of the disease conditions cited and the progenitor of the destruction of functional tissue. As cited by applicant in the specification, "In general, participation of human leucocytic elastase is postulated in catabolic processes of inflammations of various genesis". Thus contrary to applicant's assertions, it is clear that the target of the invention, as claimed is that of various inflammatory disease states. The examiner maintains the position that applicant's recognition of the inhibition of an enzyme does not minimize the fact that the prior art has recognized the anti-inflammatory ability of boswellic acid.

Howard V. Owens
Patent Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.